Debate: Επιλογή διαλύματος αναπλήρωσης όγκου

Ισορροπημένα διαλύματα

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Background

- IV fluids are the most commonly prescribed drugs in hospitals.
- Fluid therapy is a key component of the prevention and management of AKI and AKD.
- Historically, 0.9% sodium chloride (saline) has been the most commonly administered intravenous fluid.

	Balanced		Non-Balanced	
mEq/L	Normosol-R and Plasma-Lyte A	Lactated Ringers	NaCl 0.9%	Human Plasma
Na	140	130	154	136 - 145
Cl	98	109	154	96 - 106
K	5	4	0	3.5 - 5.0
Mg	3	0	0	1.5 - 2.5
Ca	0	3	0	4.5 - 5.5 (ionized)
Lactate*	0	28	0	
Acetate*	27	0	0	
Gluconate*	23	0	0	
Osmolarity	294	273	308	275 - 295
pH	~7.4	6.0-7.5	4.5-7.0	7.35-7.45

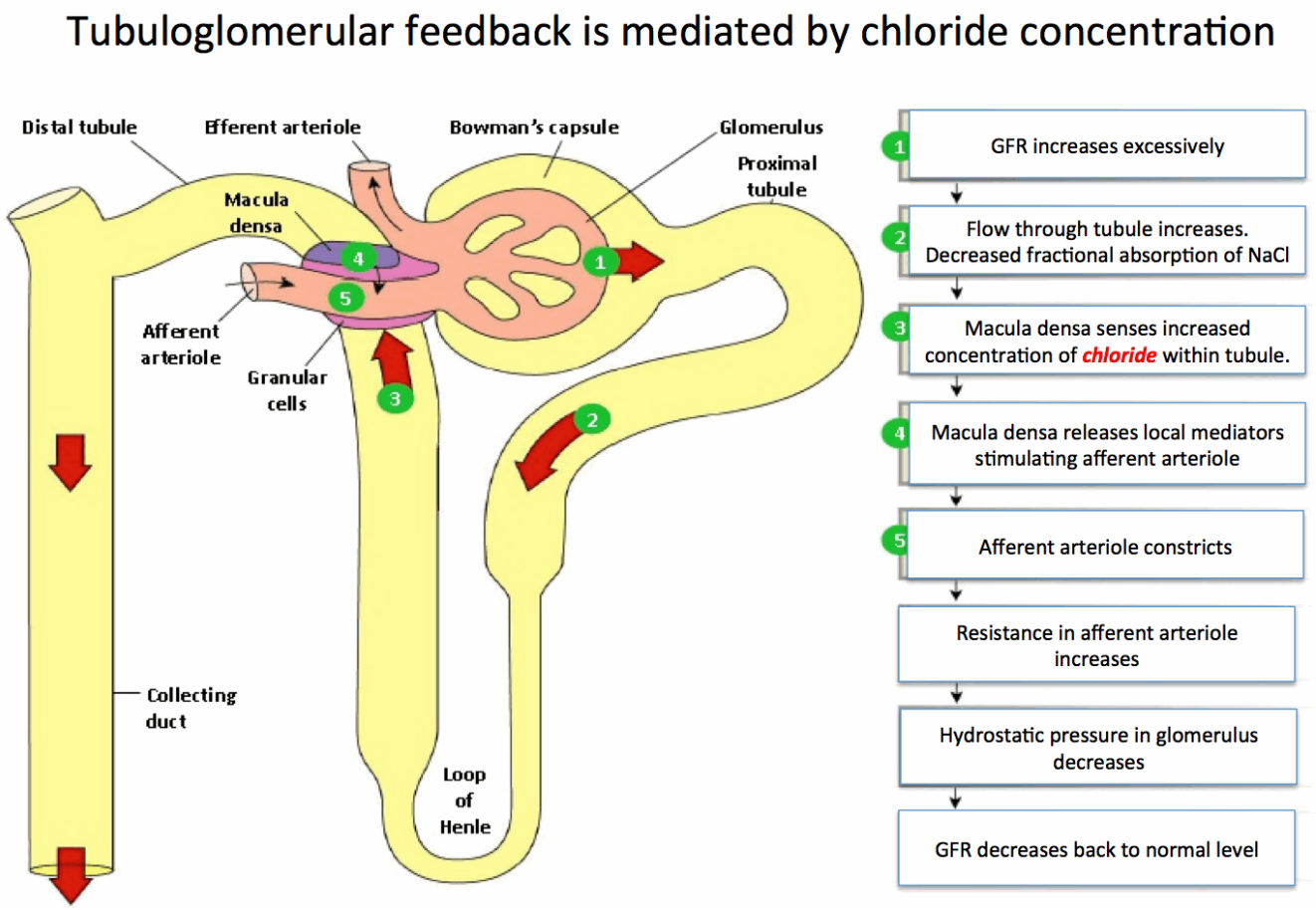
Debate

Data suggest that intravenous saline may be associated with

hyperchloremic metabolic acidosis, acute kidney injury, and death

Chloride-rich solutions may cause renal vasoconstriction and ischemia resulting in AKI

- ↑ Cl→ vasoconstriction afferent arterioles
- Auto-regulation renal blood flow and GFR.
- The renal blood flow determines the GFR or the flow of plasma filtered into the kidney.



Chloride-rich solutions may cause Hyperchloremic Metabolic Acidosis

Excess chloride→ ↓ bicarbonate

- When large amounts of chloride are infused:
- ↑ Cl^- → ↓ bicarbonate maintain electroneutrality → **metabolic acidosis**
- This is specifically a **normal anion gap (hyperchloremic) metabolic acidosis**.

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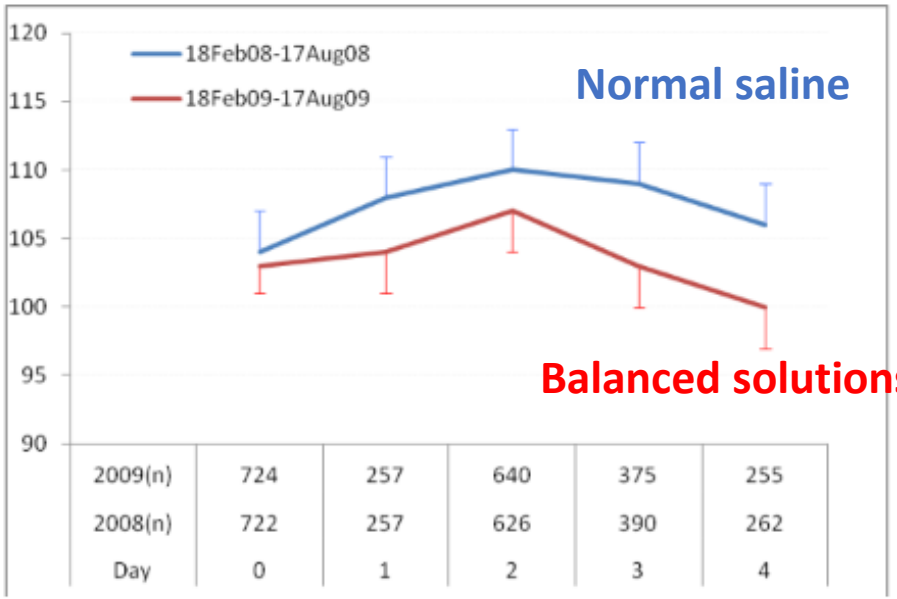
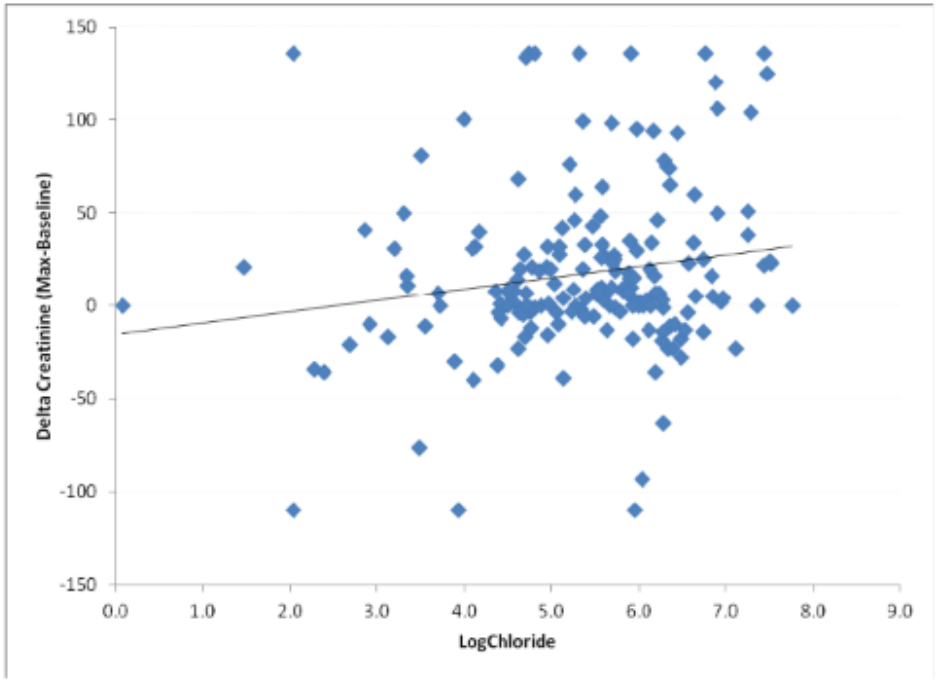
Association Between a Chloride-Liberal vs Chloride-Restrictive Intravenous Fluid Administration Strategy and Kidney Injury in Critically Ill Adults

Nor'azim Mohd Yunos, MD; Rinaldo Bellomo, MD, FCICM; Colin Hegarty, BSc; et al



29-34% CKD



Balanced solutions vs normal saline →

↓ creatinine level (P = .03; adjusted P = .007)

Yunos N. et al. JAMA 2012

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Table 3. Incidence of Acute Kidney Injury Stratified by Risk, Injury, Failure, Loss, and End-Stage (RIFLE) Serum Creatinine Criteria

	No. (%) [95% CI] of Patients[a]		
	Control Period (n = 760)	Intervention Period (n = 773)	*P* Value
RIFLE class	Normal saline	Balanced	
Risk	71 (9.0) [7.2-11.0]	57 (7.4) [5.5-9.0]	.16
Injury	48 (6.3) [4.5-8.1]	23 (3.0) [1.8-4.2]	.002
Failure	57 (7.5) [5.6-9.0]	42 (5.4) [3.8-7.1]	.10
Injury and failure	105 (14) [11-16]	65 (8.4) [6.4-10.0]	<.001

The control period was from February 18 through August 17, 2008, and the intervention period was from February 18 through August 17, 2009.

RRT use for 78 patients (10%; 95% CI, 8.1%-12%) vs 49 patients (6.3%; 95% CI, 4.6%-8.1%) (*P* = .005)

Yunos N. et al. JAMA 2012

JAMA

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Figure 1. Development of Stage 2 or 3 Acute Kidney Injury (AKI) While in the Intensive Care Unit (ICU)

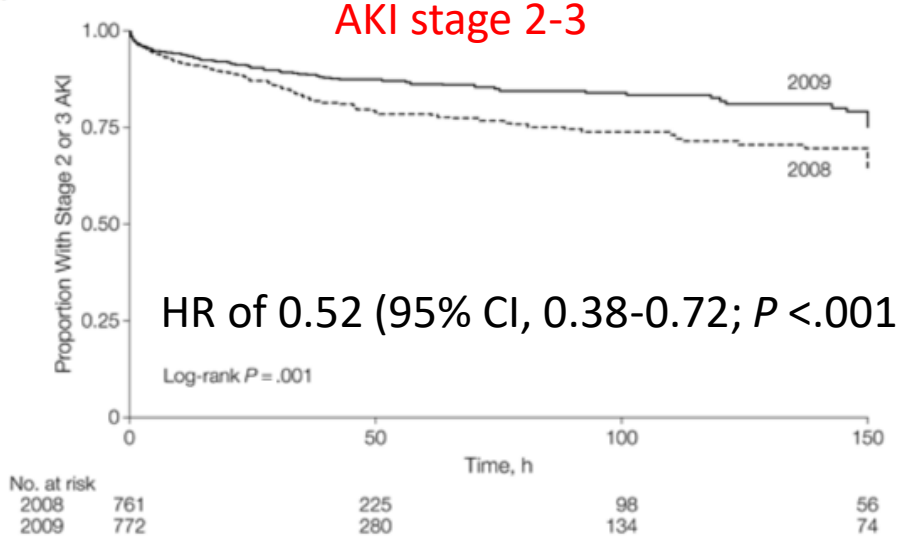
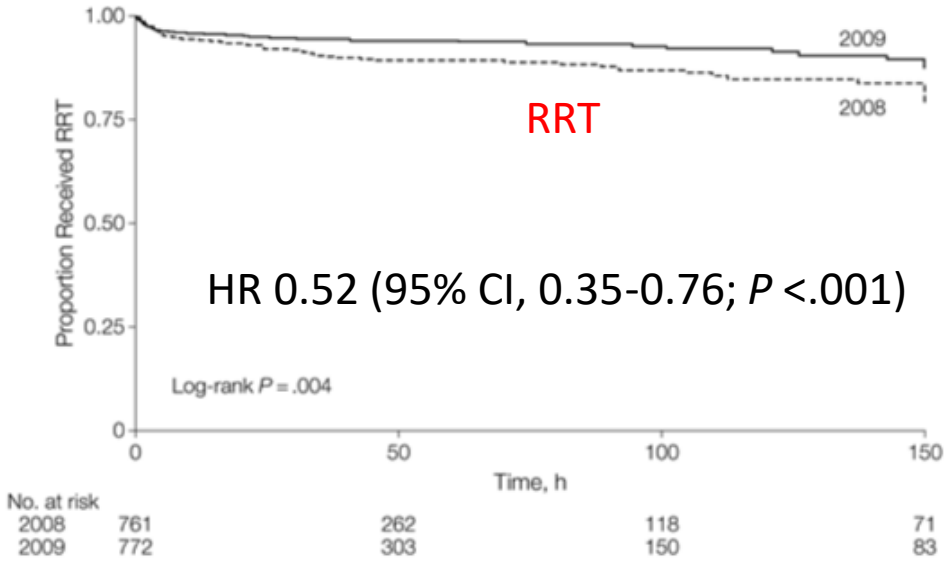


Figure 2. Renal Replacement Therapy (RRT) in the Intensive Care Unit (ICU)



no differences in long-term dialysis requirements and in non–renal medium-term outcomes or mortality, length of ICU stay

Yunos N. et al. JAMA 2012

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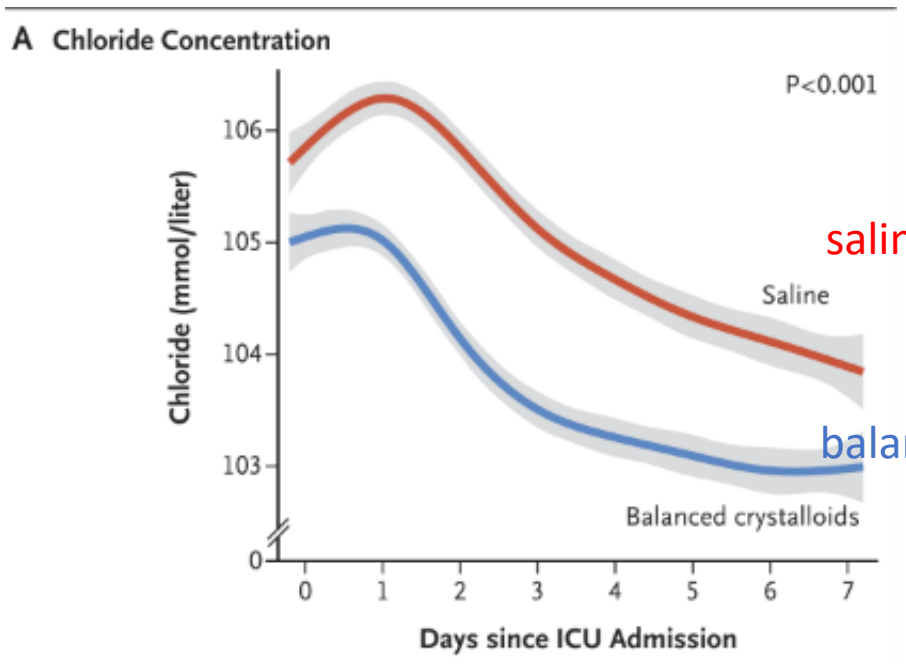
Balanced Crystalloids versus Saline in Critically Ill Adults

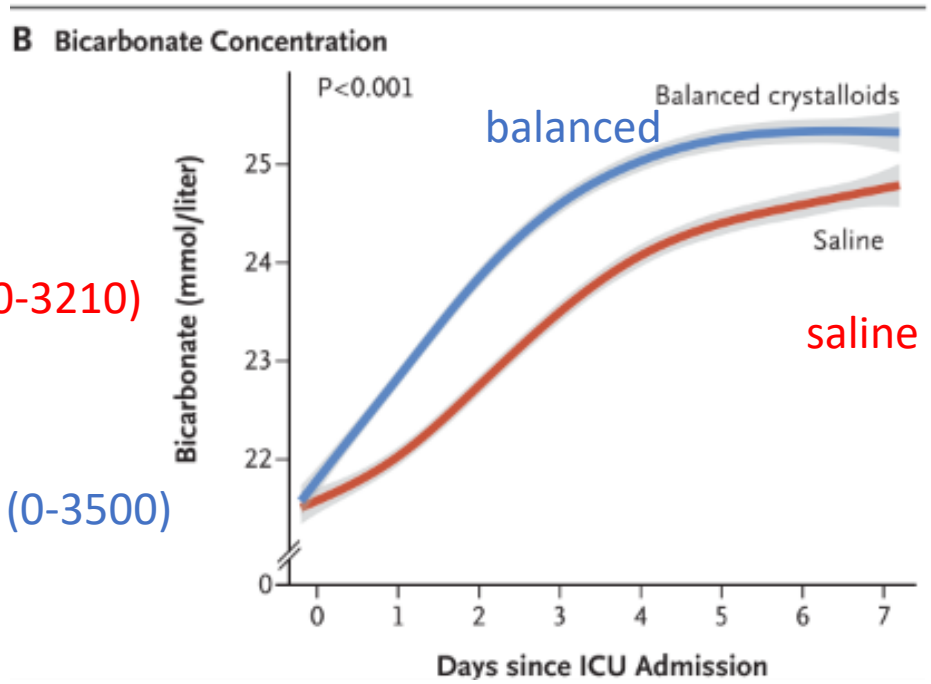


saline

1000 ml (0-3210)

balanced

1020 ml (0-3500)



balanced-crystalloids vs saline →
↓ plasma chloride > 110 mmol per liter
(24.5% vs. 35.6%, P<0.001)

balanced-crystalloids vs saline →
↓ bicarbonate < 20 mmol per liter
(35.2% vs. 42.1%, P<0.001)

Semmler M et al. NEJM 2018

CKD 17%

Table 1. Participant Characteristics at Baseline.*

Characteristic	Balanced Crystalloids (N=7942)	Saline (N=7860)
Age — yr		
Median	58	58
Interquartile range	44–69	44–69
Male sex — no. (%)	4540 (57.2)	4557 (58.0)
White race — no. (%)†	6384 (80.4)	6322 (80.4)
Weight — kg‡		
Median	80	79
Interquartile range	69–96	68–95
Coexisting renal conditions — no. (%)		
Chronic kidney disease of stage 3 or higher§	1388 (17.5)	1360 (17.3)
Previous receipt of renal-replacement therapy — no. (%)	384 (4.8)	402 (5.1)
Source of admission to ICU — no. (%)		
Emergency department	3975 (50.1)	3997 (50.9)
Operating room	1732 (21.8)	1649 (21.0)
Transfer from another hospital	1038 (13.1)	1018 (13.0)
Hospital ward	788 (9.9)	780 (9.9)
Outpatient	363 (4.6)	359 (4.6)
Another ICU within hospital	46 (0.6)	57 (0.7)
Diagnosis on ICU admission — no. (%)		
Sepsis or septic shock	1167 (14.7)	1169 (14.9)
Traumatic brain injury	698 (8.8)	665 (8.5)
Mechanical ventilation — no. (%)	2723 (34.3)	2731 (34.7)
Vasopressors — no. (%)	2094 (26.4)	2058 (26.2)
Mean predicted risk of in-hospital death — % (95% CI)¶	9.4 (9.0–9.9)	9.6 (9.2–10.0)
Baseline creatinine level — mg/dl‖		
Median	0.89	0.89
Interquartile range	0.74–1.10	0.74–1.10
Acute kidney injury of stage 2 or higher — no. (%)**	681 (8.6)	643 (8.2)

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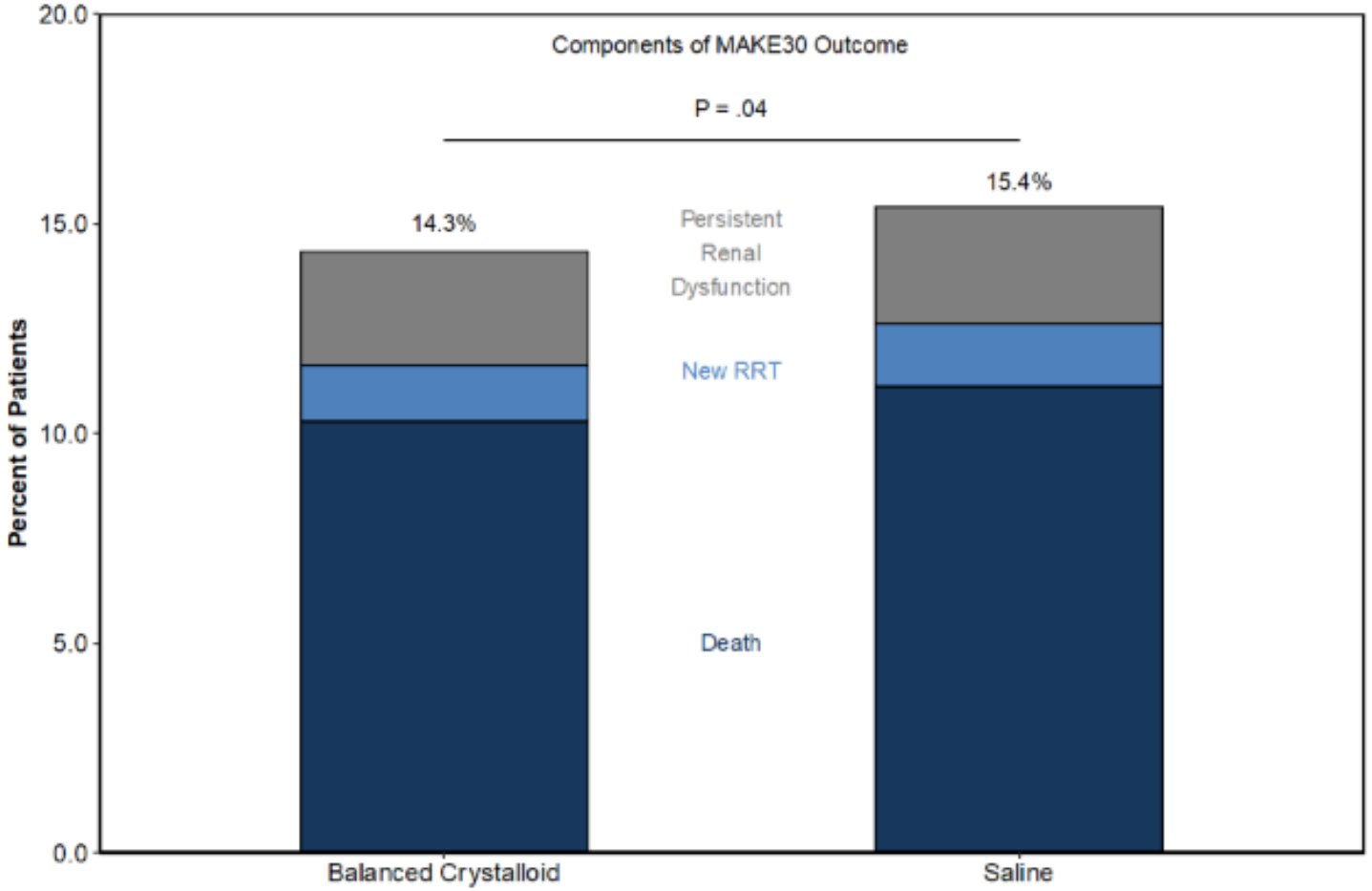


Primary Outcome:

major adverse kidney event (first 30 days)

balanced- crystalloids group vs saline →

14.3% vs 15.4%

(marginal OR, 0.91; 95% [CI], 0.84 to 0.99;

1 patient among every 94 patients admitted to an ICU

Semmler M et al. NEJM 2018

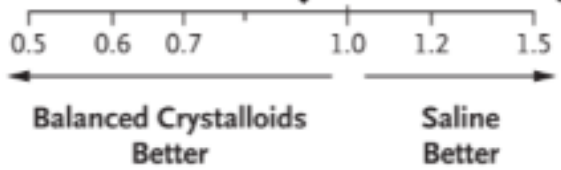
Subgroup Analysis

Subgroup	Balanced Crystalloids	Saline	Odds Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no. (%)				
Unit					0.27
Medical	615/2735 (22.5)	659/2646 (24.9)	0.87 (0.77–0.99)	0.04	
Cardiac	202/1470 (13.7)	190/1501 (12.7)	1.10 (0.89–1.36)	0.38	
Neurologic	116/1440 (8.1)	141/1377 (10.2)	0.77 (0.59–0.99)	0.04	
Trauma	131/1640 (8.0)	142/1688 (8.4)	0.95 (0.74–1.21)	0.66	
Surgical	75/657 (11.4)	79/648 (12.2)	0.93 (0.66–1.30)	0.66	
Sepsis					0.06
No	744/6775 (11.0)	756/6691 (11.3)	0.96 (0.86–1.07)	0.47	
Yes	395/1167 (33.8)	455/1169 (38.9)	0.80 (0.67–0.94)	0.01	
Traumatic brain injury					0.24
No	1034/7244 (14.3)	1118/7195 (15.5)	0.89 (0.81–0.98)	0.01	
Yes	105/698 (15.0)	93/665 (14.0)	1.09 (0.81–1.47)	0.58	
Categories of kidney function					0.19
Normal	476/5596 (8.5)	514/5561 (9.2)	0.91 (0.80–1.04)	0.16	
Acute kidney injury	315/574 (54.9)	316/537 (58.8)	0.85 (0.67–1.08)	0.18	
Chronic kidney disease	301/1388 (21.7)	307/1360 (22.6)	0.95 (0.79–1.13)	0.55	
Previous renal-replacement therapy	47/384 (12.2)	74/402 (18.4)	0.61 (0.41–0.91)	0.01	
Overall	1139/7942 (14.3)	1211/7860 (15.4)	0.91 (0.83–0.99)	0.04	

Sepsis

Kidney function

Brain injury



Sepsis, 30-day in-hospital mortality
25.2% balanced vs 29.4% saline
(aOR 0.80; 95% CI, 0.67 to 0.97; P = 0.02).

Semmler M et al. NEJM 2018

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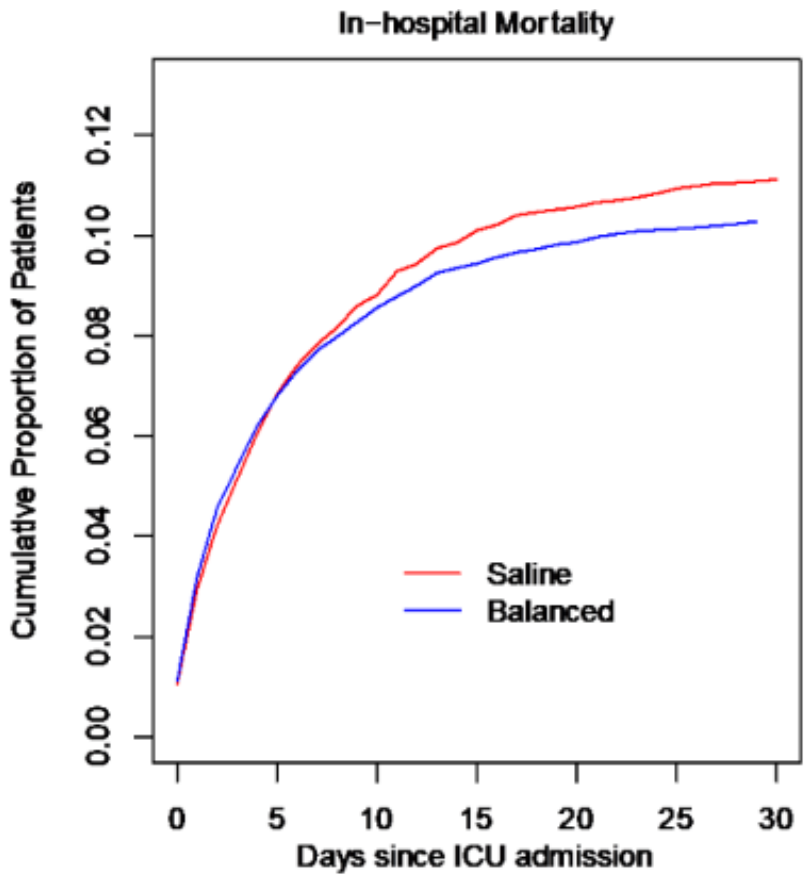

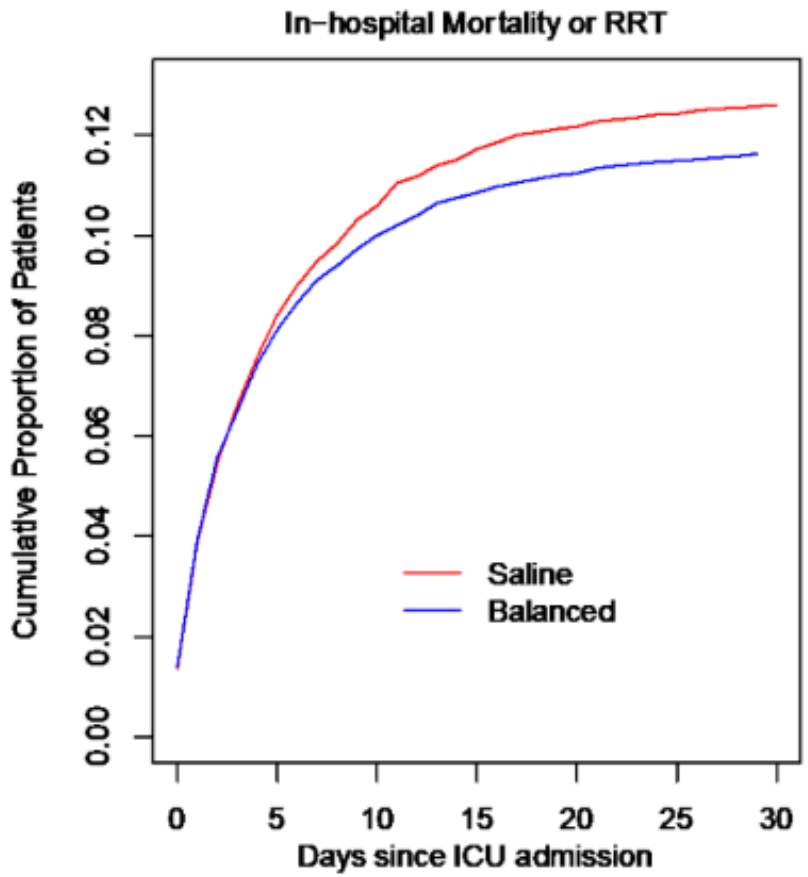

10.3% vs 11.1% (p=.006)

2.5% vs 2.9% (p=.008)

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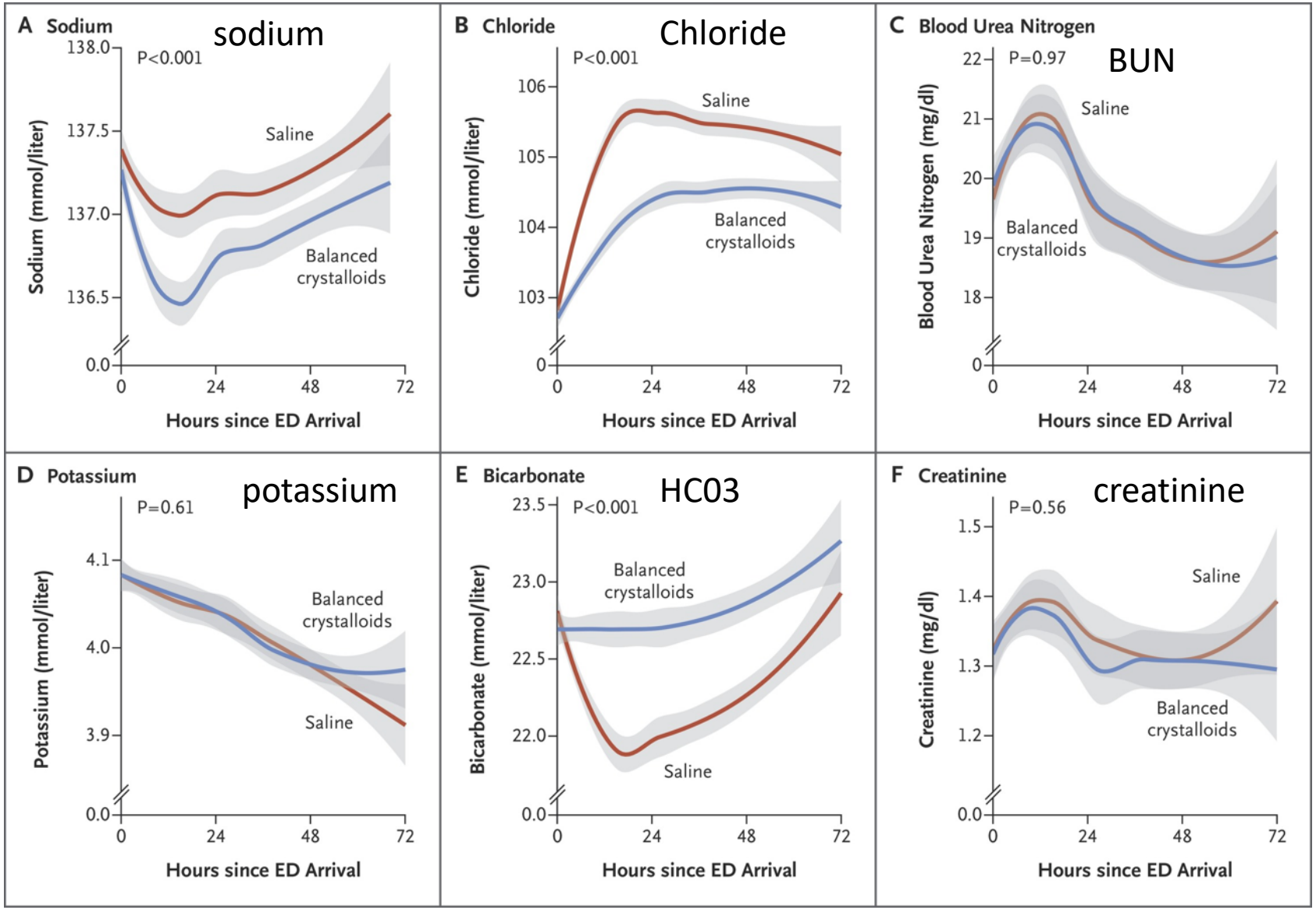
ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D., Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S., Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D., Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SALT-ED Investigators*

Self W et al. NEJM 2018

First 72 Hours after Arrival in the Emergency



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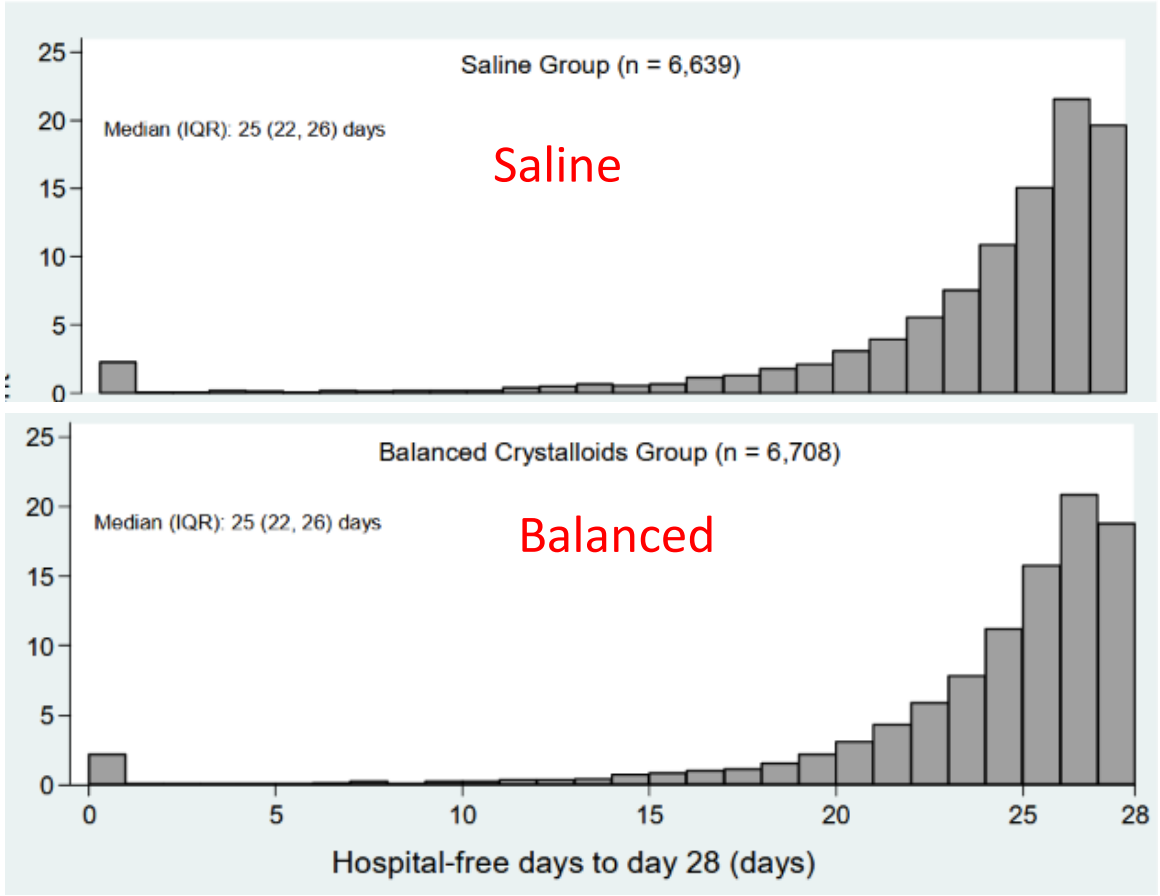
Number of hospital- free days between

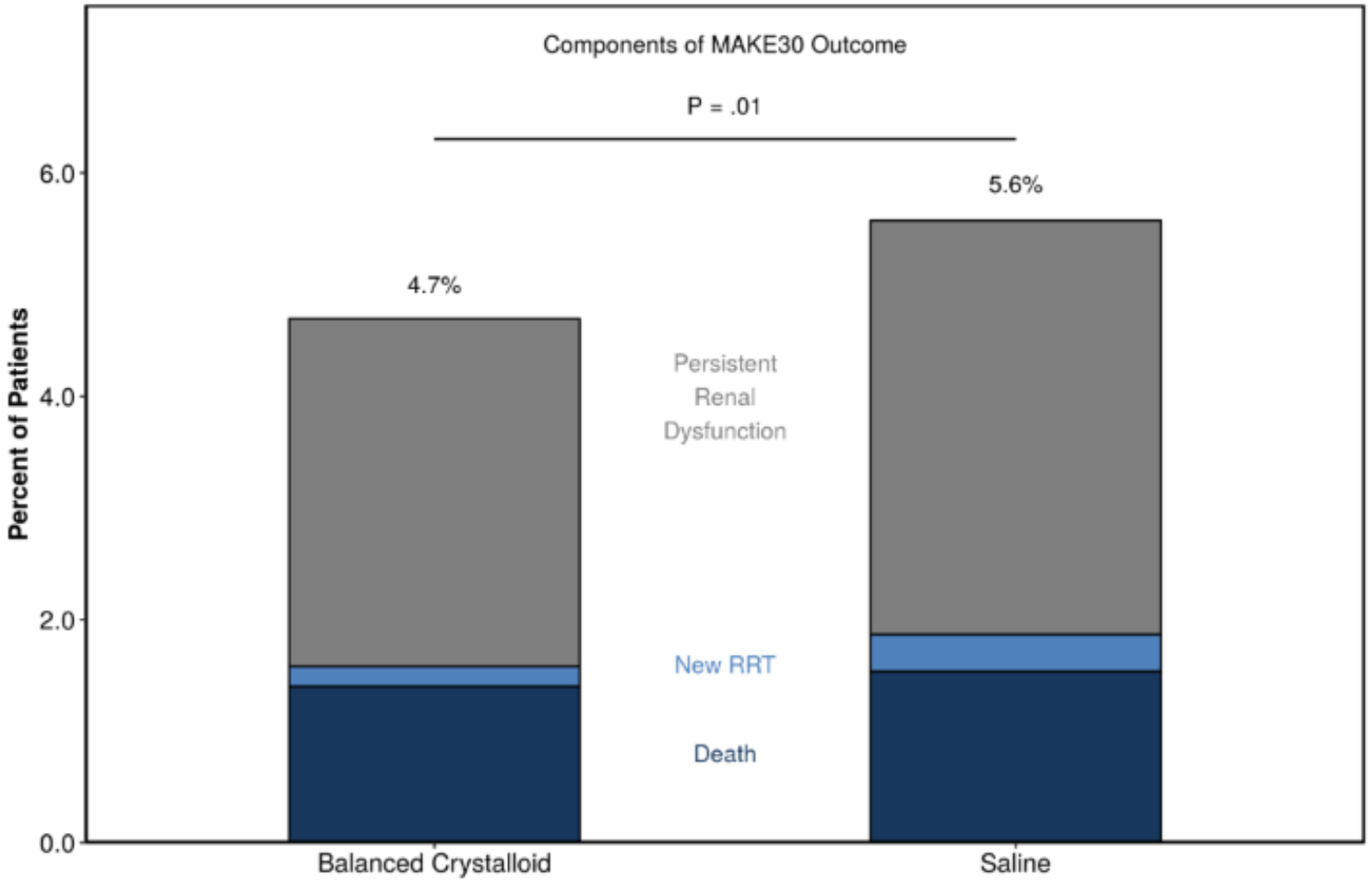
Median 25 days- **Primary outcome no difference**



hospital-free days to
day 28, a composite of in-hospital death and
hospital length of stay defined as the number of

Self W et al. NEJM 2018

Incidence of Major Adverse Kidney Events within 30 days (MAKE30)

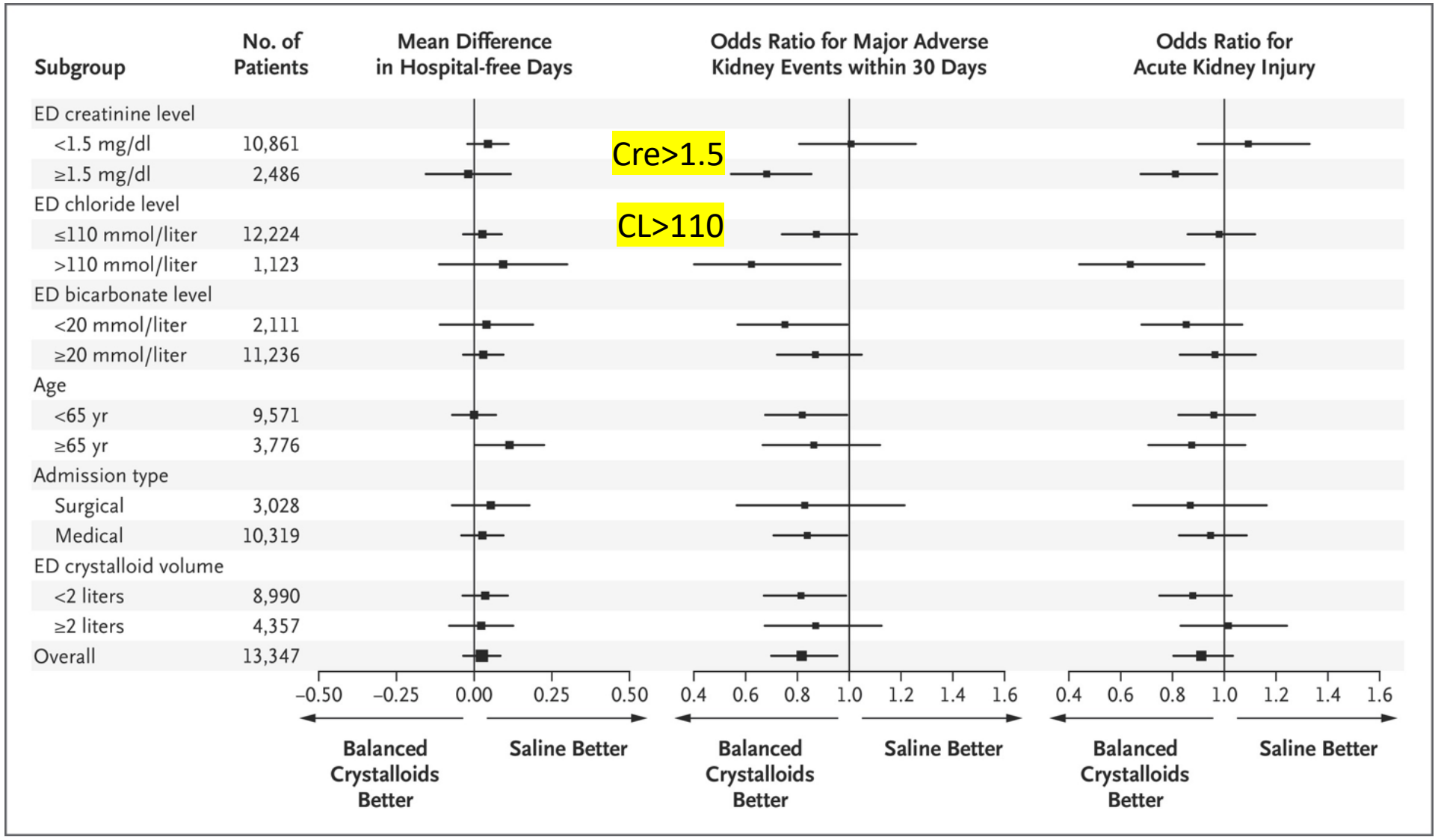


Secondary outcome

Balanced vs saline →
↓ incidence of major adverse kidney events within 30 days than those in the saline group
(4.7% vs. 5.6%;
aOR, 0.82; 95% CI, 0.70 to 0.95;
P = 0.01).

Self W et al. NEJM 2018

Higher benefit



Self W et al. NEJM 2018

Resolution of AKI

KDIGO criteria for stage 2 or higher acute kidney injury (1274 patients)

Resolution AKI

MAKE Balanced crystalloids (28.0%) vs saline group (37.6%) (P<0.001)

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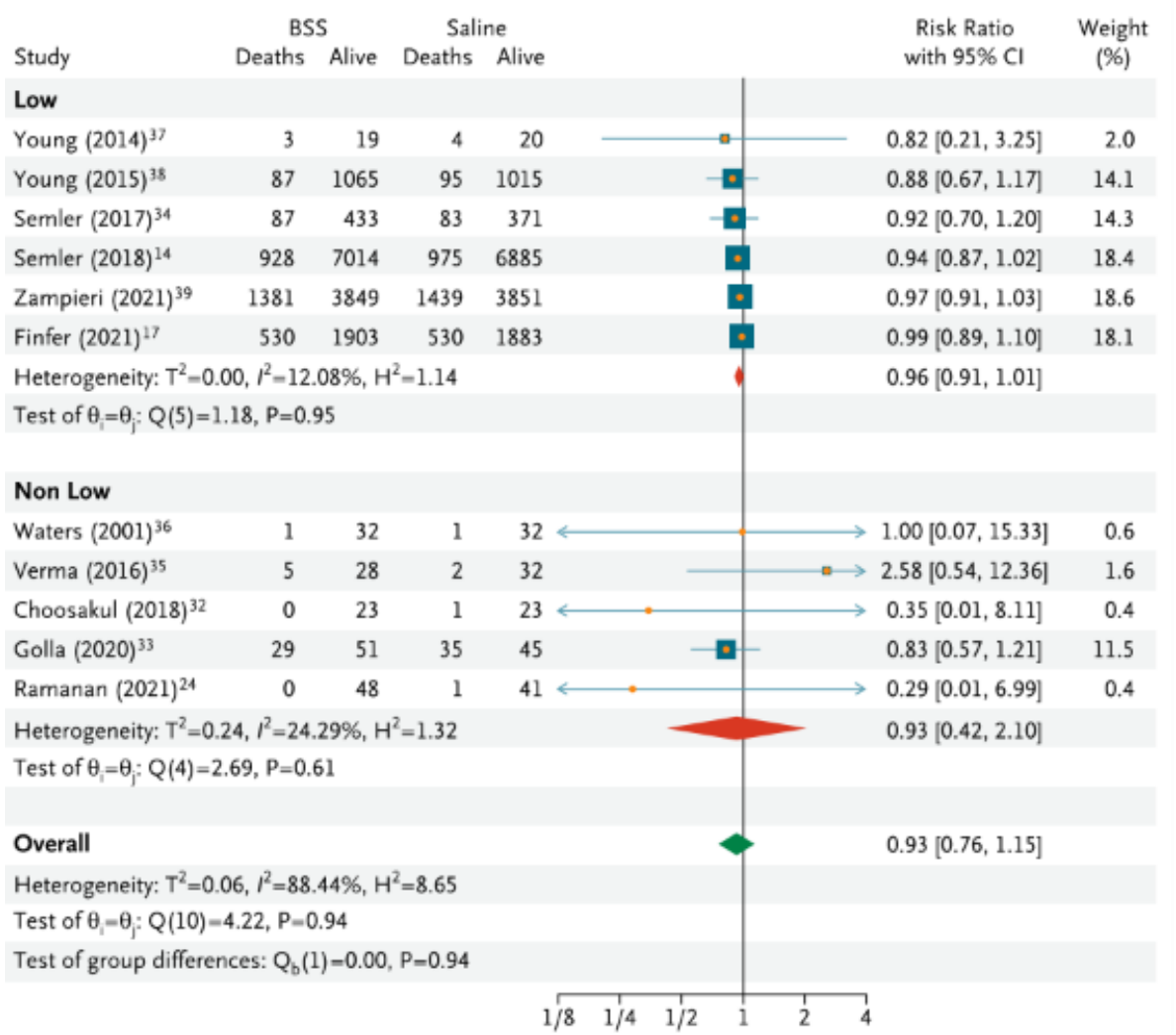
Metanalysis-
Lower 90-day mortality with buffered



Study	BSS Deaths	BSS Alive	Saline Deaths	Saline Alive	Risk Ratio with 95% CI	Weight (%)
Low						
Young (2014)[37]	3	19	4	20	0.82 [0.21, 3.25]	2.0
Young (2015)[38]	87	1065	95	1015	0.88 [0.67, 1.17]	14.1
Semler (2017)[34]	87	433	83	371	0.92 [0.70, 1.20]	14.3
Semler (2018)[14]	928	7014	975	6885	0.94 [0.87, 1.02]	18.4
Zampieri (2021)[39]	1381	3849	1439	3851	0.97 [0.91, 1.03]	18.6
Finfer (2021)[17]	530	1903	530	1883	0.99 [0.89, 1.10]	18.1
Heterogeneity: T^2=0.00, I^2=12.08%, H^2=1.14					0.96 [0.91, 1.01]	
Test of $\theta_i=\theta_j$: Q(5)=1.18, P=0.95						
Non Low						
Waters (2001)[36]	1	32	1	32	1.00 [0.07, 15.33]	0.6
Verma (2016)[35]	5	28	2	32	2.58 [0.54, 12.36]	1.6
Choosakul (2018)[32]	0	23	1	23	0.35 [0.01, 8.11]	0.4
Golla (2020)[33]	29	51	35	45	0.83 [0.57, 1.21]	11.5
Ramanan (2021)[24]	0	48	1	41	0.29 [0.01, 6.99]	0.4
Heterogeneity: T^2=0.24, I^2=24.29%, H^2=1.32					0.93 [0.42, 2.10]	
Test of $\theta_i=\theta_j$: Q(4)=2.69, P=0.61						
Overall					0.93 [0.76, 1.15]	
Heterogeneity: T^2=0.06, I^2=88.44%, H^2=8.65						
Test of $\theta_i=\theta_j$: Q(10)=4.22, P=0.94						
Test of group differences: $Q_b(1)$=0.00, P=0.94						

Primary Outcome

- ↓ mortality buffered crystalloids vs 0.9% saline RR of 0.96 (95% CI: 0.92–1.00)
- RR ↓1-9% risk of death
- Sepsis RR ↓ 1-14% risk of death

Secondary Outcome

- AKI RR 0.96 (95% CI, 0.89 to 1.02)
- RRT RR 0.95 (95% CI, 0.81 to 1.11)

Hammond N et al. NEJM Evid 2022

KDIGO

KDIGO 2026 CLINICAL PRACTICE GUIDELINE FOR ACUTE KIDNEY INJURY (AKI)AND ACUTE KIDNEY DISEASE (AKD)

PUBLIC REVIEW DRAFT
MARCH 2026

3.1 Fluid management

Recommendation 3.1.1: We recommend using crystalloids rather than colloids (albumin, gelatin, or starches) as initial management for intravascular volume expansion in children and adults at risk of or with AKI or AKD (*1B*).

Recommendation 3.1.2: We recommend using buffered crystalloids instead of 0.9% saline for volume expansion in the absence of traumatic brain injury in children and adults at risk of or with AKI or AKD (*1B*).

Exception traumatic brain injury, or prevention tumor lysis, contrast-associated AKI (in whom 0.9% saline may be preferred)

The choice of buffered crystalloid may be influenced by availability and costs.

Outcome	# Studies (Patients) [Design]	Summary of Findings		
		Certainty of Evidence	Description of Findings	Importance of Outcome
Death	21 (36387) [1,4-6] [RCT]	Moderate	**RR 0.96 (0.92, 1.00)** 8 fewer per 1000 (from 15 fewer to 0)	**Critical**
AKI	12 (29241) [1,4,7-9] [RCT]	Moderate	**RR 0.93 (0.87, 0.99)** 8 fewer per 1000 (from 14 fewer to 1 fewer)	**Critical**
AKI, Stage 3	0		No evidence	**Critical**
RRT	8 (32536) [1,10] [RCT]	Low	RR 0.92 (0.84, 1.01) 4 fewer per 1000	**Critical**

↓ 4% risk

↓ 7% risk

↓ 8% risk

Less Resource Utilization

- Retrospective propensity matched analysis
- Plasmalyte-148 vs 0.9% saline
  - Lower rates of mortality and AKI (↓ 5 times)
  - Fewer fluid (L)
  - Fewer arterial blood gas
  - Fewer lactate measurements

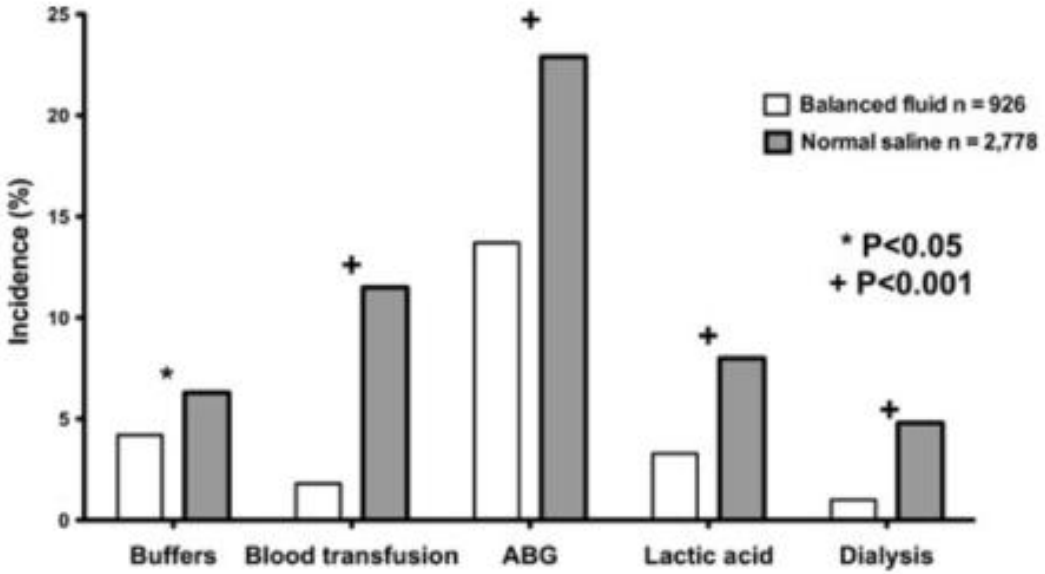


FIGURE 3. Interventions related to metaboloic acidosis diagnosis and management.

Shaw A et al. Ann Surg 2012

Conclusions

- Balanced crystalloids better preserve renal physiology
- Evidence supports lower kidney complications
- Normal saline should no longer be default therapy
- Choose fluids as carefully as any medication
- The appropriate composition of a fluid may depend on the indication for its use and the condition of the individual patient